Appl. No. : 09/904,462
Filed : July 13, 2001

REMARKS

Prior to entry of the present amendments, claims 39-51 were pending in this application, and stood rejected on various grounds. Claims 39-43, 47, 48, and 49 have been canceled, without prejudice. Claims 44, 45, 46, and 50 have been amended. The foregoing amendments in the specification and claims are of formal nature and do not introduce new matter.

Priority

According to the Office Action, although US application 09/665,350 filed on September 18, 2000 provide working examples to support the utility of PRO229, "the disclosure does not satisfy the untility/enablement requirement of 35 U.S.C. 101/112, first paragraph." Accordingly, the Examiner accorded the filing date of July 13, 2001 as the earliest priority date of the present application.

Applicants respectfully disagree. Applicants rely on the chondrocyte re-differentiation assay results (Example 95) to establish substantial and specific asserted utility for the polypeptide PRO229 PCT/US00/04414 filed on February 22, 2000. Accordingly, the present application is submitted to be entitled to at least the priority date of February 22, 2000. It is noted that in parallel application Serial No. 09/906618, claiming nucleic acid encoding the polypeptides of the present application, the Examiner acknowledged that the chondrocyte redifferentiation results established patentable utility, and determined that February 22, 2000 was the effective filing date. The same conclusion should be reached in the present application.

Title

The title was objected to as "not descriptive." The new title added by the foregoing amendment is believed to overcome this objection.

Appl. No. : **09/904,462**
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Specification and claims

The specification was objected to for its recitation of "T cell surface glycoproteins CD6 and CD6." The foregoing amendment to the specification corrects this typographical error.

The specification was further objected to since the ATCC deposit number recited in claims 39-44 did not match the deposit number listed in the specification. Since the claims no longer contain a reference to the deposit number, and the information provided in the specification is correct, the present objection is believed to be moot.

Claims 31-48 were objected to for identifying a nucleotide sequence by a figure with SEQ ID NO in parenthesis. Applicants note that the claims in the present application are directed to polypeptide and not nucleotide sequences, and prior to entry of the current amendment, the application contained claims 39-51. Accordingly, Applicants assume that the present objection concerns polypeptide claims 39-51. As the claims have been amended to refer solely to appropriate SEQ ID NO, the withdrawal of the present objection would be in order.

Objections and Rejections under 35 U.S.C. §§101 and 112

(1) Claims 39-51 were rejected under 35 U.S.C. 101 "because the claimed invention is not supported by a credible, substantial, and specific, or a well-established utility."

Applicants respectfully disagree, and traverse the rejection.

Applicants rely on the ability of the claimed polypeptides the induce chondrocyte redifferentiation (Example 95) to establish patentable utility.

It was well known at the effective filing date of the present application that chondrocytes play a key role in the synthesis and maintenance of the articular cartilage, which in turn is essential to normal joint function. Unfortunately, compared to many other tissues, articular cartilage essentially lacks the ability to regenerate following injury. One way of achieving

cartilage repair, for example in osteoarthritis, is to harvest human articular chrondrocytes (HACs) from non-affected, healthy areas of the joint to be repaired. The HACs are subsequently grown in monolayer cell culture in order to produce sufficient amount of cells to fill the articular defect. Condrocytes found in healthy joints have a round shape, and express high levels of extracellular matrix molecules, such as aggrecan, type II collagen, and link protein. In contrast, monolayer cultures of chondrocytes produce dedifferentiated fibroblast-like structures, similar to those found in the cartilage of aging and arthritic joints. (See, e.g. Zhang et al., *Experimental Cell Research* 263:33-42 (2001) – copy enclosed). Accordingly, agents that are capable of inducing chondrocyte redifferentiation are useful in providing properly differentiated chrondrocytes in monolayer cell cultures, which can be used in the treatment of joint diseases (See, e.g. Schnabel et al., Osteoarthritis and Cartilage, 10(1):62-70 (2002) – copy enclosed). In addition, molecules capable of chondrocyte redifferentiation are promising drug candidates to repair aging or arthritic joints, for example, in which the chondrocytes have been dedifferentiated.

With regard to the chondrocyte redifferentiation assay the Examiner notes that although PRO229 tested "positive" in this assay, the result is ambiguous, since without further details (e.g the difference between positive and negative controls, to what stage the cell differentiated, how many cells survived or dead in each group, etc) one of ordinary skill in the art "would not know hot to use the claimed invention based on that result."

Example 95 clearly states that after performing the assay as described in the Example, including 5 days of incubation at 37 °C, a picture of each well was taken and the differentiation state of the chondrocytes was determined. "A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control." As discussed above, chondrocyte redifferentiation results in a clear difference in the shape of the chondrocytes. Accordingly, one skilled in the art at the priority date of the present application had no difficulty determining whether redifferentiation has taken place, simply following the steps of Example 95.

According to the applicable legal standard, if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered

credible by a person of ordinary skill in the art, the rejection based on lack of utility is inappropriate. According to M.P.E.P. 2107 II (B) (1) (ii), "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of records . . . that is probative of the applicant's assertions." Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

The Examiner cited no reasons in support of a position that the logic underlying the utility asserted in the present application would be seriously flawed. Since one skilled in the art would recognize that the asserted utility is "credible" without the required additional technical detailed, the Examiner is respectfully requested to withdraw the present rejection.

The remaining claims have been amended to recite that the polypeptide encoded by the claimed nucleic acid are "capable of inducing chrondrocyte redifferentiation." Since the reason for the Examiner's finding that enablement was not provided within the full scope of the claims was the absence of functional limitation in the claims, Applicants submit that the claims as currently amended are fully enabled. Indeed, the *in vitro* data provided in the specification coupled with general knowledge in the art at the time the invention was made provide sufficient guidance to one skilled in the art to use the invention without undue experimentation.

(2) Claims 39-51 were rejected under 35 U.S.C. § 112, first paragraph. According to the rejection, "since the claimed invention is not supported by ... a specific, substantial or credible utility..., one skilled in the art clearly would not know how to use the claimed invention." The Examiner further added, "*even if* the specification taught how to use the PRO229 polypeptide, enablement would not be commensurate i scope with claims 39-51."

As discussed above, the claimed invention is supported by a specific, substantial, and credible asserted utility. In addition, the claims no wrecite polypeptide comprising the PRO229 polypeptide sequence of SEQ ID NO: 148, with or without the associated signal sequence. The

specification provides specific examples for making and using such polypeptides, accordingly, the reconsideration and withdrawal of the present rejection is respectfully requested.

(3) Claims 39-51 were rejected under 35 U.S.C. § 112, second paragraph as "indefinite" in their recitation of the "extracellular domain." Since this term is no longer present in the claims, the rejection is moot.

Rejections Over Prior Art

The rejections are based on the assumption that the effective filing date of the present application is July 13, 2001. As discussed above, the effective filing date of the present application should be properly February 22, 2000.

(1) Claims 39-51 were rejected under 35 U.S.C. §102(b) as "anticipated" by Wood et al., WO 99/14328.

WO 99/14328 was published on March 25, 1999, which is less than a year before the effective filing date of the present application, therefore, WO 99/14328 is not a reference under 35 U.S.C. 102(b). Nor does Wood et al. anticipate the claimed invention under 35 U.S. C. 102(a).

In *In re Wilder*, the court acknowledged that an application claiming a certain compound could avoid the anticipatory effect of a prior publication specifically naming the same compound by showing that the claimed compound has "properties completely different from those attributed to them by the reference description." 419 F.2d 447, 451, 166 USPQ 545 (C.C.P.A. 1970).

WO 99/14328 discloses the PRO229 polypeptide of SEQ ID NO: 148. According to information provided on pages 21-22, the PRO polypeptides show homology to scavenger receptors, which, in turn, are known to protect IgG molecules from catabolic degradation. According to page 75, lines 24-32, the PRO229 polypeptide is a newly identified member of the family containing scavenger receptor homology, and thus possesses immune function and/or segments which resist degradation, typical of this family. Accordingly, WO 99/14328 attributes

to PRO229 properties that are completely different from the properties on which the utility of PRO299 is based, and which are now recited in the claims. Therefore, Wood et al. does not anticipate the claimed invention under 35 U.S.C. 102(a).

(2) Claims 39-44, 47, 50 and 51 were rejected under 35 U.S.C. 102(b) as allegedly anticipated by Gebe et al. WO 98/39443.

The cancellation of claims 39-43, and 47 moots their rejection. The remaining claims now recite polypeptides comprising PRO229, SEQ ID NO: 148, with or without the associate signal peptide, therefore, they are not anticipated by Gebe et al.

Applicants note the documents cited but not relied upon in support of any of the rejections.

All claims pending in this application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should the Examiner find that there are any further issues outstanding, she is invited to contact the undersigned attorney at the telephone number indicated below in order to facilitate the allowance of the present application.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**."

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Respectfully submitted,

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Version with markings to show changes made

In the Specification:

The title has been canceled and replaced with the following new title: --PRO229 polypeptides.--

The paragraph starting at page 106, line 1 has been canceled and replaced with the following new paragraph:

--The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO229. In particular, Applicants have identified and isolated cDNA encoding a PRO229 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO229 polypeptide have significant homology with antigen wc1.1, M130 antigen, and T cell surface glycoprotein CD6. It also is related to Sp-alpha. Accordingly, it is presently believed that PRO229 polypeptide disclosed in the present application is a newly identified member of the family containing scavenger receptor homology, a sequence motif found in a number of proteins involved in immune function and thus possesses immune function and /or segments which resist degradation, typical of this family. --

In the Claims:

Claims 39-43, 47, 48, and 49 have been canceled.

Claims 44, 45, 46, and 50 have been amended as follows:

44. (Once amended) An isolated polypeptide comprising:

(a) the amino acid sequence of the polypeptide [shown in Figure 54 (SEQ ID NO: 148)} of SEQ ID NO: 148; or

(b) the amino acid sequence of the polypeptide [shown in Figure 54 (SEQ ID NO: 148)] of SEQ ID NO: 148, lacking its associated signal peptide[;

(c) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 54 (SEQ ID NO: 148);

(d) the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 54 (SEQ ID NO: 148), lacking its associated signal peptide; or

(e) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209377],

wherein said polypeptide induces chondrocyte proliferation.

45. (Once amended) The isolated polypeptide of claim 44 comprising the amino acid sequence of the polypeptide [shown in Figure 54 (SEQ ID NO: 148)] of SEQ ID NO: 148.

46. (Once amended) The isolated polypeptide of claim 44 comprising the amino acid sequence [shown in Figure 54 (SEQ ID NO: 148)] of the polypeptide of SEQ ID NO: 148, lacking its associated signal peptide.

50. (Once amended) A chimeric polypeptide comprising a polypeptide according to Claim [39] 44 fused to a heterologous polypeptide.